

=> file .meeting

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FILE 'BIOTECHNO' ENTERED AT 16:11:52 ON 21 MAY 2004

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=> insulin(P) (chemiluminescent or chemiluminescence) (P) antibody

L1 0 FILE AGRICOLA

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'INSULIN(P) (CHEMILUMI'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'INESCENCE) (P) ANTIBODY'

L2 12 FILE BIOTECHNO

L3 0 FILE CONFSCI

L4 0 FILE HEALSAFE

L5 0 FILE IMSDRUGCONF

L6 0 FILE LIFESCI

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'INSULIN(P) (CHEMILUMI'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'INESCENCE) (P) ANTIBODY'

L7 0 FILE MEDICONF

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'INSULIN(P) (CHEMILUMI'

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH

FIELD CODE - 'AND' OPERATOR ASSUMED 'INESCENCE) (P) ANTIBODY'

L8 8 FILE PASCAL

TOTAL FOR ALL FILES

L9 20 INSULIN(P) (CHEMILUMINESCENT OR CHEMILUMINESCENCE) (P) ANTIBODY

=> dup rem  
ENTER L# LIST OR (END):19  
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.  
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE  
PROCESSING COMPLETED FOR L9  
L10 16 DUP REM L9 (4 DUPLICATES REMOVED)

=> d l10 ibib abs total

L10 ANSWER 1 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
ACCESSION NUMBER: 2001:34102182 BIOTECHNO  
TITLE: Human milk contains detectable levels of  
immunoreactive leptin  
AUTHOR: Lyle R.E.; Kincaid S.C.; Bryant J.C.; Prince A.M.;  
McGehee Jr. R.E.  
CORPORATE SOURCE: R.E. Lyle, Department of Pediatrics, Univ. of Arkansas  
for Med. Sciences, Arkansas Children's Hospital,  
Little Rock, AR 72202, United States.  
SOURCE: Advances in Experimental Medicine and Biology, (2001),  
501/- (87-92), 29 reference(s)  
CODEN: AEMBAP ISSN: 0065-2598  
DOCUMENT TYPE: Journal; Conference Article  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AN 2001:34102182 BIOTECHNO  
AB Leptin, the recently cloned product of the obese (ob) gene, is a  
16kDa-protein that acts as a circulating satiety factor. It also serves  
to regulate energy expenditure and may act as a counter regulatory  
hormone to **insulin**. Initially thought to be exclusively  
produced by mature adipocytes, its mRNA has now been identified in  
significant levels in the placenta as well as the fetus raising  
speculation regarding its importance as a growth factor. Given studies  
demonstrating that exclusively breastfed infants are leaner due to  
decreased energy intakes than formula-fed infants, we hypothesized that  
the presence of leptin in human milk could participate in mediating the  
earlier satiety of those infants fed human milk. We undertook this  
initial study to qualitatively examine the presence of leptin in human  
milk utilizing an immunoblot approach. Random milk samples during the  
first 2 weeks of lactation were available for study from 4 mothers  
delivering at term. Milk samples were centrifuged, the aqueous layer  
removed, and the protein content quantitated. One-hundred micrograms of  
total protein were separated by sodium dodecyl sulfate-polyacrylamide-gel  
electrophoresis (SDS-PAGE), transferred to nitrocellulose, and  
immunoblotted with an antileptin **antibody**. As controls,  
recombinant human leptin alone and a sample of milk containing added  
leptin were similarly electrophoresed and immunoblotted. Labeled proteins  
were visualized by **chemiluminescence**. Significant amounts of  
leptin protein were identified in all milk samples examined. No  
difference in protein detection was identified in fresh milk vs. frozen  
milk, and little difference was apparent in foremilk samples vs. hindmilk  
samples. These preliminary data reveal the presence of leptin in term  
human milk and suggest that further studies to document bioactivity of  
milk-derived leptin are warranted.

L10 ANSWER 2 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
ACCESSION NUMBER: 2001:34701927 BIOTECHNO  
TITLE: Commercial assays available for **insulin**-like  
growth factor I and their use in diagnosing growth  
hormone deficiency  
AUTHOR: Clemons D.R.  
CORPORATE SOURCE: Prof. D.R. Clemons, Division of Endocrinology,  
University of North Carolina, CB# 7170, 6111  
Thurston-Bowles, Chapel Hill, NC 275990-7170, United

States.  
E-mail: endo@med.unc.edu  
SOURCE: Hormone Research, (2001), 55/SUPPL. 2 (73-79), 20  
reference(s)  
CODEN: HRMRA3 ISSN: 0301-0163  
DOCUMENT TYPE: Journal; Conference Article  
COUNTRY: Switzerland  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AN 2001:34701927 BIOTECHNO  
AB Radioimmunoassays of **insulin**-like growth factor I (IGF-I) are commonly used for screening adults and children for growth hormone (GH) deficiency or excess. There are, however, many problems with such assays. Attempts to resolve these problems have focused on methods of separating IGF-I from its binding proteins, and on reducing inter- and intra-assay variability. In particular, the collection of sufficient high-quality normative data is a major difficulty in many laboratories. Clinical evaluation of assays is also problematic. IGF-I levels vary with age after puberty, and this is complicated by the maintenance of IGF-binding protein 3 levels by IGF-II. Generally, studies have shown that IGF-I is sensitive and specific for the diagnosis of acromegaly, but screening for GH deficiency (GHD) is less precise. The most commonly used commercial assays are immunoradiometric (IRMA) sandwich assays, using **antibodies** specific to IGF-I. IRMA assays are quick and accurate, and the two-site **antibody** reactivity produces a high degree of specificity. Additional techniques such as acid-ethanol extraction or saturation with IGF-II can improve reliability. More recently, the introduction of **chemiluminescence** has provided enhanced speed and sensitivity. The clinical use of these assays has provided a wealth of information regarding the diagnosis of GHD, and it may be possible to reduce the number of patients who require provocative GH testing. IGF-I assays are also of great use in monitoring GH replacement therapy. Despite the problems, IGF-I measurement is currently the best indirect method available for screening and monitoring patients with GHD.  
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L10 ANSWER 3 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
DUPLICATE  
ACCESSION NUMBER: 2000:30614926 BIOTECHNO  
TITLE: Fully automated **chemiluminescence**  
immunoassay of **insulin** using  
**antibody** - Protein A - Bacterial magnetic  
particle complexes  
AUTHOR: Tanaka T.; Matsunaga T.  
CORPORATE SOURCE: T. Matsunaga, Department of Biotechnology, Tokyo Univ.  
of Agric and Technol., Koganei, Tokyo 184-8588, Japan.  
E-mail: tmatsuna@cc.tuat.ac.jp  
SOURCE: Analytical Chemistry, (01 AUG 2000), 72/15 (3518-3522)  
CODEN: ANCHAM ISSN: 0003-2700  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AN 2000:30614926 BIOTECHNO  
AB We report a fully automated sandwich immunoassay for the determination of human **insulin** using **antibody**-protein A-bacterial magnetic particle (BMP) complexes and an alkaline phosphatase-conjugated secondary anti-body. BMPs bearing protein A-MagA inserted on the external surface of the membrane were prepared in tire Magnetospirillum sp. AMB-1 transconjugant for a protein A-magA fusion gene. MagA protein was used as an anchor to attach protein A onto the membrane. Protein A-BMP complexes harvested from transconjugant AMB-1 were subsequently complexed with anti-human **insulin antibodies** by specific binding between the Z domain of protein A and the Fc component of IgG to form the

**antibody**-protein A-BMP complexes. The complexes were quite monodisperse after the binding of the **antibody**. The BMPs' monodispersity resulted in high signal and low noise in the immunoassay. The luminescence intensity ((kilocounts/s)/ $\mu$ g of **antibody**) from **antibody**-protein A-BMP complexes after immunoreaction was higher than that from BMPs chemically conjugated to an **antibody**. This was explained by a difference in dispersion. The fully automated sandwich immunoassay system using **antibody**-protein A-BMP complexes made possible precise assays of human **insulin** in serum.

L10 ANSWER 4 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
DUPLICATE

ACCESSION NUMBER: 1999:30647040 BIOTECHNO  
TITLE: Growth hormone (GH) receptor blockade with a PEG-modified GH (B2036-PEG) lowers serum **insulin**-like growth factor-I but does not acutely stimulate serum GH  
AUTHOR: Thorner M.O.; Strasburger C.J.; Wu Z.; Straume M.; Bidlingmaier M.; Pezzoli S.S.; Zib K.; Scarlett J.C.; Bennett W.F.  
CORPORATE SOURCE: Dr. M.O. Thorner, Department of Medicine, Box 466, Univ. of Virginia Hlth. Sci. Center, Charlottesville, VA 22908, United States.  
E-mail: mot@virginia.edu  
SOURCE: Journal of Clinical Endocrinology and Metabolism, (1999), 84/6 (2098-2103), 19 reference(s)  
CODEN: JCEMAZ ISSN: 0021-972X

DOCUMENT TYPE: Journal; Article  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AN 1999:30647040 BIOTECHNO  
AB B2036-PEG, a GH receptor (GH-R) antagonist, is an analog of GH that is PEG-modified to prolong its action. Nine mutations alter the binding properties of this molecule, preventing GH-R dimerization and GH action. A potential therapeutic role of B2036-PEG is to block GH action, e.g. in refractory acromegaly. A phase I, placebo-controlled, single rising-dose study was performed in 36 normal young men (ages, 18-37 yr; within 15% ideal body weight). Four groups received a single sc injection of either placebo (n = 3 in each group, total n = 12) or B2036-PEG (0.03, 0.1, 0.3, or 1.0 mg/kg; n = 6 each dose). B2036-PEG and GH concentrations were measured 0, 0.25, 0.5, 1, 3, 6, 9, 12, 24, 36, 48, 72, 96, 120, and 144 h after dosing. Serum **insulin**-like growth factor-I was measured before and 1-7 days after dosing. All doses were well tolerated, with no serious or severe adverse reactions. B2036-PEG, at 1.0 mg/kg, reduced **insulin**-like growth factor-I by 49  $\pm$  6% on day 5 (P < 0.001 vs. placebo). GH was measured by two independent methods: 1) modified Nichols **chemiluminescence** assay (empirically corrected for B2036-PEG cross-reactivity); and 2) direct GH two-site immunoassay, using monoclonal **antibodies** that did not react with B2036-PEG. There was good agreement between the two methods. GH did not change substantially at any B2036-PEG dose, suggesting that B2036-PEG does not interact with hypothalamic GH-Rs to block short-loop feedback. B2036-PEG may thus block peripheral GH action without enhancing its secretion.

L10 ANSWER 5 OF 16 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED.  
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ACCESSION NUMBER: 2000-0085606 PASCAL  
COPYRIGHT NOTICE: Copyright .COPYRGT. 2000 INIST-CNRS. All rights reserved.  
TITLE (IN ENGLISH): Heme-undecapeptide labeling on **insulin** for the immunoassay of **insulin** with **chemiluminescence** detection

AUTHOR: ZAITSU K.; KIMURA Y.; OHBA Y.; HAMASE K.; MOTOMURA Y.; ITOSE M.; ISHIYAMA M.

CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Kyushu University, Maidashi, Higashi, Fukuoka 812-8582, Japan

SOURCE: Analytical sciences, (1999), 15(9), 871-878, 14 refs.

DOCUMENT TYPE: Journal

BIBLIOGRAPHIC LEVEL: Analytic

COUNTRY: Japan

LANGUAGE: English

AVAILABILITY: INIST-20879, 354000081190350110

AN 2000-0085606 PASCAL

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AB Heme-undecapeptide (HUP, microperoxidase-11) labeled **insulins**, in which the Lys(3) amino group of HUP was cross-linked to one amino group of **insulin** (Gly(A1), Phe(B1) or Lys(B29)) via a disulfide linkage, were prepared. Lys(3)-[3-(2-pyridyldithio) propionoyl]-HUP (Lys(3)-PDP-HUP) was synthesized by the reaction of HUP with N-succinimidyl 3-(2-pyridyldithio)propionate and then conjugated with Gly(A1)-thioglycoloyl- (Gly(A1)-TG-), Phe(B1)-TG- or Lys(B29)-TG- **insulin**. Each TG-**insulin** was generated by deacetylation of Gly(A1)-acetylthioglycoloyl- (Gly(A1)-ATG-), Phe(B1)-ATG- or Lys(B29)-ATG-**insulin**, that was prepared by reacting native **insulin**, Phe(B1)-3,4,5,6-tetrahydronaphthalenyl-**insulin** (Phe(B1)-THP-**insulin**) or Gly(A1), Phe(B1)-(THP).sub.2-**insulin** with N-succinimidyl S-acetylthioacetate (SATA), respectively, followed by deprotection of THP, a reversible amino-protecting group. Both preparative reversed-phase and anion-exchange HPLC were used in the syntheses of PDP-HUP and the **insulin** derivatives (THP-, ATG- and HUP-**insulin**), respectively. The optimal reaction conditions for these syntheses were extensively studied using HPLC separation. In addition, immunoreactivity of Phe(B1)-HUP-**insulin** was manifested by using a solid-phase antibody method with chemiluminescence detection.

L10 ANSWER 6 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
DUPLICATE

ACCESSION NUMBER: 1999:29394103 BIOTECHNO

TITLE: Human **insulin** receptor and **insulin** signaling proteins in hepatic disease

AUTHOR: Spector S.A.; Olson E.T.; Gumbs A.A.; Friess H.; Buchler M.W.; Seymour N.E.

CORPORATE SOURCE: Dr. N.E. Seymour, Surgical Service (112), VA Connecticut Healthcare System, 950 Campbell Avenue, West Haven, CT 06516, United States.

SOURCE: Journal of Surgical Research, (01 MAY 1999), 83/1 (32-35), 20 reference(s)

DOCUMENT TYPE: CODEN: JSGRA2 ISSN: 0022-4804

COUNTRY: Journal; Conference Article

LANGUAGE: United States

SUMMARY LANGUAGE: English

AN 1999:29394103 BIOTECHNO

AB **Insulin** regulates hepatocellular metabolism and growth following **insulin** receptor (IR) autophosphorylation and activation of the intracellular adapter protein, **insulin** receptor substrate 1 (IRS-1). IRS-1 activates SH2 domain proteins such as Grb2, which may be vital to hepatocyte growth. To determine if these substances are abnormally expressed under pathophysiologic conditions, IR, IRS-1, Grb2 protein, and IR mRNA were studied in normal human liver (n = 10), cirrhotic liver (n = 10), and hepatocellular carcinoma (HCC) (n = 10) that had been procured during operative procedures. IR mRNA was quantified by S1-nuclease assay using a 195-bp digoxigenin-labeled IR DNA probe and normalized to the level of expression of the glyceraldehyde 3-

phosphate dehydrogenase (GAPDH) gene. Protein concentrations were determined by immunoblot analysis following SDS-PAGE of liver homogenate samples. Labeled DNA and antibody-complexed protein were detected by chemiluminescent means and quantified by densitometric analysis (mean densitometric units  $\pm$  standard error). Similar levels of IR mRNA were observed in normal tissue, cirrhosis, and HCC. IR protein concentration was significantly greater in HCC than in normal liver ( $1.82 \pm 0.2$  vs  $1.25 \pm 0.17$ ;  $P < 0.05$ ). IRS-1 was significantly increased in cirrhosis compared to normal liver ( $1.61 \pm 0.31$  vs  $0.86 \pm 0.21$ ;  $P < 0.05$ ). No differences were observed in Grb2 in the three tissue types. Insulin receptor overexpression, previously seen in other tumor types, may confer an insulin-mediated growth advantage in HCC if added receptors reflect functional high affinity binding sites. Although an altered mass of IRS-1 protein was not observed in HCC, an IRS-1 increase in cirrhosis may favor hepatic regeneration.

L10 ANSWER 7 OF 16 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED.  
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ACCESSION NUMBER: 1999-0070051 PASCAL  
COPYRIGHT NOTICE: Copyright .COPYRGT. 1999 INIST-CNRS. All rights reserved.

TITLE (IN ENGLISH): Elevated insulin-like growth factor-I and transforming growth factor- $\beta$ 1 and their receptors in patients with idiopathic hypertrophic obstructive cardiomyopathy : A possible mechanism. Commentary  
Cardiovascular surgery 1997

AUTHOR: GUANGMING LI; LI R.-K.; MICKLE D. A. G.; WEISEL R. D.; MERANTE F.; BALL W. T.; CHRISTAKIS G. T.; CUSIMANO R. J.; WILLIAMS W. G.; SPINALE F. G. (comment.)  
WEISEL Richard D. (ed.)

CORPORATE SOURCE: Centre for Cardiovascular Research, The Toronto Hospital, General Division, University of Toronto, Toronto, Ontario, Canada; Division of Cardiovascular Surgery, The Toronto Hospital, General Division, University of Toronto, Toronto, Ontario, Canada; Department of Clinical Biochemistry, The Toronto Hospital, General Division, University of Toronto, Toronto, Ontario, Canada; Cardiothoracic Surgery and Physiology, Medical University of South Carolina, Charleston, SC, United States  
American Heart Association. Council on Cardio-Thoracic and Vascular Surgery, United States (patr.)  
Circulation : (New York), (1998), 98(19, SUP), II.144-II.150, 33 refs.

SOURCE: Conference: Council on Cardio-Thoracic and Vascular Surgery. American Heart Association. Scientific Sessions, Orlando, Florida (United States), 9 Nov 1997  
ISSN: 0009-7322 CODEN: CIRCAZ

DOCUMENT TYPE: Journal; Conference; Article; Commentary

BIBLIOGRAPHIC LEVEL: Analytic

COUNTRY: United States

LANGUAGE: English

AVAILABILITY: INIST-5907, 354000070713770250

AN 1999-0070051 PASCAL  
CP Copyright .COPYRGT. 1999 INIST-CNRS. All rights reserved.

AB Background-Idiopathic hypertrophic obstructive cardiomyopathy (HOCM) is characterized by regional myocardial hypertrophy. In our previous study, we demonstrated that mRNA levels for insulin-like growth factor-I (IGF-I) and transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1) were elevated in HOCM tissue. In this study, we investigated IGF-I and TGF- $\beta$ 1 protein levels and their respective receptor levels and localization. Methods and Results-Myocardial growth factor protein levels were quantified with the use of chemiluminescent slot blot

analysis with monoclonal **antibodies** against IGF-I and TGF- $\beta$ . The growth factor receptor binding sites were evaluated with  $^{125}\text{I}$ -labeled IGF-I and TGF- $\beta$ 1. The receptors were localized with immunohistochemistry. Data were expressed as mean $\pm$ SEM. IGF-I and TGF- $\beta$  protein levels in HOCM myocardium (351.8 $\pm$ 46.5 and 17.4 $\pm$ 2.0 ng/g tissue, respectively; n=6) were significantly higher (P<0.01 for all groups) than in non-HOCM myocardium obtained from patients with aortic stenosis (AS, 182.1 $\pm$ 22.7 and 8.0 $\pm$ 1.2 ng/g tissue, respectively; n = 5), stable angina (SA, 117.4 $\pm$ 20.9 and 7.5 $\pm$ 2.7 ng/g tissue, respectively; n=5), and transplanted hearts (TM, 166.3 $\pm$ 30.1 and 6.4 $\pm$ 1.2 ng/g tissue, respectively; n=5). Maximal and high-affinity binding sites for IGF-I receptor in the HOCM were greater (P<0.01 and P<0.05) than the levels in AS, SA, and TM. The maximal receptor binding sites for TGF- $\beta$ 1 in HOCM were greater (P<0.05) than those for SA and TM. Immunohistochemistry demonstrated that IGF-I and TGF- $\beta$ 1 receptors were located on the cardiomyocytes and TGF- $\beta$ 1 receptors were located on the fibroblasts.

**Conclusions**-Increased IGF-I and TGF- $\beta$ 1 gene expression previously observed in HOCM myocardium results in elevated protein levels. IGF-I and TGF- $\beta$ 1 signals may be further amplified by increased receptor numbers on cardiomyocytes and fibroblasts. The data suggest a possible autocrine mechanism of TGF-I-stimulated cardiomyocyte hypertrophy and a paracrine mechanism of TGF- $\beta$ 1-stimulated extracellular matrix overproduction in HOCM.

L10 ANSWER 8 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
ACCESSION NUMBER: 1997:27180840 BIOTECHNO  
TITLE: Quantification of insulin-like growth factor I (IGF-I) without interference by IGF binding proteins  
AUTHOR: De Leon D.D.; Asmerom Y.  
CORPORATE SOURCE: D.D. De Leon, Department of Physiology, Loma Linda Univ. School of Medicine, Loma Linda, CA 92350, United States.  
SOURCE: Endocrinology, (1997), 138/5 (2199-2202), 16 reference(s)  
CODEN: ENDOAO ISSN: 0013-7227  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AN 1997:27180840 BIOTECHNO  
AB A **chemiluminescent** dot blot assay has been developed by our laboratory for rapid determinations of IGF-I in serum-free conditioned media (CM) collected from cultured cells. In contrast to IGF-I radioimmunoassays (RIAs), the IGF binding proteins (IGFBPs) did not interfere with the dot blot assay and did not require the laborious (and sometimes ineffective) removal of IGFBPs. Although all six IGFBPs were shown to bind to  $^{125}\text{I}$  IGF-I, none interfered with IGF-I detection on nitrocellulose dot blots. In contrast, an RIA using the same Oncogene monoclonal **antibody** (clone 82-9A) showed interference by IGFBP-1, IGFBP-2, and IGFBP-4. The IGF-I dot blot assay was sensitive (0.125 - 8.0 ng IGF-I), specific (assay crossreactivity with IGF-II is less than 1%), and reproducible (intra-assay variance <=6%; inter-assay variance < 12%) when **chemiluminescence** was quantified by phosphorimager and Molecular Analyst software (BioRad). The apparent sensitivity of the enhanced **chemiluminescence** (ECL) reagent to serum, precludes the use of this assay for IGF-I determination in serum or in serum-containing media.

L10 ANSWER 9 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
ACCESSION NUMBER: 1997:27330650 BIOTECHNO  
TITLE: Detection of serum insulin-like growth factor binding proteins on Western ligand blots by biotinylated IGF and enhanced

AUTHOR: **chemiluminescence**  
De Beeck L.O.; Verlooy J.E.A.; Van Buul-Offers S.C.;  
Du Caju M.V.L.

CORPORATE SOURCE: L.O. De Beeck, Department of Pediatrics, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium.

SOURCE: Journal of Endocrinology, (1997), 154/2 (R1-R5), 16 reference(s)

DOCUMENT TYPE: CODEN: JOENAK ISSN: 0022-0795

COUNTRY: Journal; Article

LANGUAGE: United Kingdom

SUMMARY LANGUAGE: English

AN 1997:27330650 BIOTECHNO

AB A novel procedure for the detection of IGF binding capacity of IGFBPs on Western ligand blots (WLB) was developed using biotinylated IGFs as probes. The biotinylated IGF-IGFBP complexes were visualized by streptavidin- horseradish peroxidase and enhanced **chemiluminescence** (ECL). The procedure was found to be faster and more efficient than the conventional method with iodinated IGFs. In normal human serum a predominant doublet at 38-42 kDa and five smaller bands at 35, 34, 30, 28 and 24 kDa were detected by both methods, whereas two additional bands at 26 and 16 kDa became visible with the ECL method. In pregnancy serum only one single faint band at 30 kDa could be detected by the iodinated method. In contrast, the ECL method revealed five other bands at 42, 34, 28, 26 and 16 kDa. Besides the 38-42 kDa doublet, the 30 and 16 kDa bands reacted strongly with anti-IGFBP-3 **antibodies** in Western immunoblotting (WIB) and therefore were related to IGFBP-3 fragments. The technical advantages of this ECL method include an extremely short exposure time to the radiographic film and a long stability of the probe. In addition, the ECL method is a non-radioactive method, making radioprotection and radioactive waste removal unnecessary.

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ACCESSION NUMBER: 1997-0415170 PASCAL

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TITLE (IN ENGLISH): Detection of serum **insulin-like growth factor** binding proteins on Western ligand blots by biotinylated IGF and enhanced **chemiluminescence**

AUTHOR: DE BEECK L. O.; VERLOOY J. E. A.; VAN BUUL-OFFERS S. C.; DU CAJU M. V. L.

CORPORATE SOURCE: Department of Pediatrics, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium; Utrecht University/Wilhelmina Children's Hospital, PB 18009, 3501 CA Utrecht, Netherlands

SOURCE: Journal of endocrinology, (1997), 154(2), R1-R5, 16 refs.

DOCUMENT TYPE: ISSN: 0022-0795 CODEN: JOENAK

BIBLIOGRAPHIC LEVEL: Journal; Short communication

COUNTRY: Analytic

LANGUAGE: United Kingdom

AVAILABILITY: English

AN 1997-0415170 PASCAL

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AB A novel procedure for the detection of IGF binding capacity of IGFBPs on Western ligand blots (WLB) was developed using biotinylated IGFs as probes. The biotinylated IGF-IGFBP complexes were visualized by streptavidin-horseradish peroxidase and enhanced **chemiluminescence** (ECL). The procedure was found to be faster and more efficient than the conventional method with iodinated IGFs. In normal human serum a predominant doublet at 38-42 kDa and five smaller

bands at 35, 34, 30, 28 and 24 kDa were detected by both methods, whereas two additional bands at 26 and 16 kDa became visible with the ECL method. In pregnancy serum only one single faint band at 30 kDa could be detected by the iodinated method. In contrast, the ECL method revealed five other bands at 42, 34, 28, 26 and 16 kDa. Besides the 38-42 kDa doublet, the 30 and 16 kDa bands reacted strongly with anti-IGFBP-3 **antibodies** in Western immunoblotting (WIB) and therefore were related to IGFBP-3 fragments. The technical advantages of this ECL method include an extremely short exposure time to the radiographic film and a long stability of the probe. In addition, the ECL method is a non-radioactive method, making radioprotection and radioactive waste removal unnecessary.

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ACCESSION NUMBER: 1996-0493621 PASCAL  
COPYRIGHT NOTICE: Copyright .COPYRGT. 1996 INIST-CNRS. All rights reserved.  
TITLE (IN ENGLISH): Regulation of hepatic **insulin** receptors by pancreatic polypeptide in fasting and feeding  
AUTHOR: SEYMOUR N. E.; VOLPERT A. R.; ANDERSEN D. K.  
CORPORATE SOURCE: Department of Surgery, Veterans Affairs Medical Center, Dallas, Texas, United States; Department of Surgery, Veterans Affairs Medical Center, West Haven, Connecticut 06516, United States; University of Texas Southwestern Medical Center, Dallas, Texas, United States; Yale University School of Medicine, New Haven, Connecticut, United States  
SOURCE: The Journal of surgical research, (1996), 65(1), 1-4, 17 refs.  
Conference: Annual Meeting of the Association for Academic Surgery, Dearborn, Michigan (United States), 8 Nov 1995  
ISSN: 0022-4804 CODEN: JSGRA2  
DOCUMENT TYPE: Journal; Conference  
BIBLIOGRAPHIC LEVEL: Analytic  
COUNTRY: United States  
LANGUAGE: English  
AVAILABILITY: INIST-9554, 354000066645520010  
AN 1996-0493621 PASCAL  
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AB Pancreatic polypeptide (PP) increases hepatic **insulin** receptor (IR) binding activity in fasted PP-deficient rats, but not fasted normal animals. PP-induced alteration of hepatic IR levels in normal animals may be detectable in the fed state when IR concentrations are lower than during fasting. In the current study, the effect of exogenous PP on IR concentrations in the fed and fasted states was determined in healthy 300- to 350-g male Sprague-Dawley rats. Ten animals were administered PP 100 µg/kg/day for 3 days by intraperitoneal injection and 10 weight-matched control animals received saline vehicle. Five PP- and five saline-administered rats were fasted for 12 hr prior to organ procurement, while 5 PP- and 5 saline-treated rats were given free access to food for this period. Livers were removed and snap-frozen. IRs were isolated from solubilized hepatocyte membranes by affinity chromatography with agarose-bound wheat germ agglutinin. Western blots were performed using a specific **antibody** to the β subunit of the IR, which was detected by a **chemiluminescence** technique after 45-min exposure to X-ray film. Exposed films were examined by scanning densitometry and IR concentration was expressed as absorbance units per milligram of hepatic protein (mean ± SE). Statistical comparisons were by Student's t test with significance taken at P < 0.05. Feeding was associated with a significantly lower IR concentration in saline-administered animals compared with the fasted state (24.2 ± 4.0 vs 53.3 ± 11.1). PP administration in fed rats resulted in significantly increased IR concentration as compared with that seen in

saline-administered fed animals ( $43.8 \pm 8.9$  vs  $24.2 \pm 4.0$ ). This difference may be due to increased IR synthesis with long-term PP administration, and supports the role of PP as a regulatory factor in hepatic carbohydrate metabolism.

L10 ANSWER 12 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
DUPLICATE  
ACCESSION NUMBER: 1994:24110762 BIOTECHNO  
TITLE: Direct detection of **insulin**-like growth factor II (IGF-II) by chemiluminescence without interference by IGF binding proteins  
AUTHOR: De Leon D.D.; Terry C.; Nissley S.P.  
CORPORATE SOURCE: Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, United States.  
SOURCE: Endocrinology, (1994), 134/4 (1960-1963)  
CODEN: ENDOAO ISSN: 0013-7227  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AN 1994:24110762 BIOTECHNO  
AB A dot blot method for the detection of picogram quantities of human and rat **insulin**-like growth factor II (IGF-II) in serum-free conditioned media is described. The crossreactivity of human recombinant IGF-I in the assay was <10%. None of the IGF binding proteins (IGFBP 1-6) diminished the IGF-II signal. In contrast, significant interference by the IGFBPs was observed when the same concentrations of IGFBPs and  $^{125}\text{I}$ -IGF-II were used in a radioimmunoassay which utilized the same **antibody**. Why IGF-II is detected in the dot blot assay without IGFBP interference is not understood. We speculate that the conformation of the IGF-II/binding protein complex may be altered by binding to the nitrocellulose, exposing the IGF-II epitope that is recognized by the **antibody**. IGF-II was detected in 1  $\mu\text{l}$  of serum-free conditioned media from BRL 3A cells (which secrete IGF-II) while no signal was generated by 50  $\mu\text{l}$  of BRL 3A2 conditioned media (which do not secrete IGF-II). In summary, this method is ideal for screening cells in serum free-culture for production of IGF-II without the need for separation of IGF-II from cell derived IGFBPs.

L10 ANSWER 13 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
ACCESSION NUMBER: 1994:24122599 BIOTECHNO  
TITLE: Development of hormone assay methods  
AUTHOR: Miyachi Y.  
CORPORATE SOURCE: First Dept. of Internal Medicine, Toho University School of Medicine, Tokyo, Japan.  
SOURCE: Kakuigaku, (1994), 31/3 (283-288)  
CODEN: KAIGBZ ISSN: 0022-7854  
DOCUMENT TYPE: Journal; General Review  
COUNTRY: Japan  
LANGUAGE: Japanese  
SUMMARY LANGUAGE: English; Japanese  
AN 1994:24122599 BIOTECHNO  
AB Before the introduction of radioimmunoassay, most hormones were measured by bioassay and/or chemical methods. The sensitivity of these methods was low, so large amounts of samples were needed to perform hormone determination. In 1959, Berson and Yalow, first applied radioimmunoassay to the measurement of **insulin**, after which many protein hormones were determined by this method. Subsequently, radioimmunoassays were developed for small peptide molecules as well as for non-peptide hormones such as thyroid hormones and steroid hormones. Two site immunoradiometric assay in which one **antibody** was immobilized and another labeled with  $^{125}\text{I}$  becomes popular, due to its high sensitivity and the development of monoclonal **antibody**.

production by the hybridoma technique. Although radioimmunoassays immunoradiometric assays are sensitive and robust techniques, there has been a growing interest for non-isotopic alternatives since early 1980s. Recently, non-isotopic immunoassay methods utilizing **chemiluminescence**, fluorescence and enzymes as labels are widely used. **Chemiluminescence** immunoassays, fluorescence immunoassays and enzymic immunoassays with fluorometric detection have resulted in sensitivities adequate to replace radioimmunoassays. Since hormone immunoassays are all dependent upon immunologic properties of hormones, the simultaneous measurement of hormones by a biologic method sometimes shows discrepancies in the hormone concentrations. Hormone assay methods employing biologically specific receptors was introduced, but used not so widely due to the instability of hormone receptors. *In vitro* bioassay, is easy to perform and has high sensitivity and applicable for definite hormones. Isotopic and non-isotopic immunoassays are simple and quite useful, but other methods such as radioreceptor assay and bioassay-especially *in vitro* bioassay are also recommendable to run with radioimmunoassays.

L10 ANSWER 14 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
ACCESSION NUMBER: 1994:24229892 BIOTECHNO  
TITLE: Protease-induced alteration of **insulin-like**  
growth factor binding protein-3 as detected by  
radioimmunoassay. Agreement with ligand blotting data  
AUTHOR: Lassarre C.; Lalou C.; Perin L.; Binoux M.  
CORPORATE SOURCE: INSERM U 142, Hopital Saint Antoine, 184, rue du  
Faubourg St Antoine, 75571 Paris Cedex 12, France.  
SOURCE: Growth Regulation, (1994), 4/2 (48-55)  
CODEN: GREGEP ISSN: 0956-523X  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United Kingdom  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AN 1994:24229892 BIOTECHNO  
AB Structural alteration of **insulin-like** growth factor binding protein-3 (IGFBP-3) resulting from limited proteolysis by one or more serine proteases *in vivo* was first described in the serum of pregnant women and in certain pathological conditions. Western immunoblotting has since been employed to detect the phenomenon in normal serum, using a polyclonal **antibody** raised against recombinant human IGFBP-3 and a highly sensitive technique of visualization by **chemiluminescence**. The major proteolytic fragment of 30 kDa, which fails to be detected in native serum by ligand blotting owing to its weak affinity for IGFs, has proved clearly visible in all serum samples tested, sometimes accompanied by smaller fragments of 20 and 16 kDa. Among the serum samples analysed, increasing proportions of proteolysed IGFBP-3 were found in the following order: acromegalic patients, normal subjects, GH-deficient patients, pregnant women. In RIAs done with the same **antibody**, many of the serum samples yielded dose-response curves which were not parallel with standard curves, with lower gradients. In the samples where measurements were possible, apparent IGFBP-3 levels proved lower in pregnant women ( $2.28 \pm 0.23$  mg/l, mean  $\pm$  SEM) than in normal adults ( $4.26 \pm 0.33$  mg/l,  $P < 0.001$ ). These observations, which contradict earlier reports of higher levels in pregnant women, suggest that the 30 kDa proteolytic fragment has a weaker affinity for the **antibody** than the intact IGFBP-3 (which in ligand- and immunoblotting appears as a characteristic 42-39 kDa doublet and which is barely or not detectable in pregnancy serum). The diminished affinity of the 30 kDa IGFBP-3 fragment was confirmed by an experiment incubating pregnancy serum with normal serum at 37°C. Here, the progressive proteolysis of intact IGFBP-3 in normal serum coincided with the gradual decrease in immunoassayable IGFBP-3 concentrations. Conversely, in a women after delivery and in 2 cases of Laron's syndrome under rhIGF-I therapy, the reappearance or

increase of the 42-39 kDa band (intact IGFBP-3) in ligand blotting coincided with an increase in immunoassayable IGFBP-3 levels. Scatchard analysis of the results of competitive binding experiments provided proof of this difference in affinity. Recombinant IGFBP-3 had approximately 10 times the affinity of pregnancy serum IGFBP-3 for the **antibody**. Furthermore, acromegalic serum proved to have two types of site, one of high, and one of low, affinity, which correspond to the intact and proteolysed forms. Since the limited proteolysis of IGFBP-3 does not disrupt the ternary 150 kDa complexes, our results show that the protease-induced structural changes are recognized by the **antibody** within the complexes in native serum. Finally, this study shows that the results of IGFBP-3 measurement by RIA depend on the relative affinities of the **antibody** for the intact and proteolysed forms of the protein and they should therefore be interpreted with caution.

L10 ANSWER 15 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
ACCESSION NUMBER: 1993:23295212 BIOTECHNO  
TITLE: Streptavidin blotting: A sensitive technique to study cell surface proteins; Application to investigate autophosphorylation and endocytosis of biotin-labeled **insulin** receptors  
AUTHOR: Levy-Toledano R.; Caro L.H.P.; Hindman N.; Taylor S.I.  
CORPORATE SOURCE: National Institutes of Health, Building 10, Bethesda, MD 20892, United States.  
SOURCE: Endocrinology, (1993), 133/4 (1803-1808)  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AN 1993:23295212 BIOTECHNO  
AB Covalent attachment of biotin provides a useful method to label cell surface proteins. Subsequent to biotinylation, the protein can be purified by immunoprecipitation with a specific **antibody**, followed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. After transfer to a membrane by electroblotting, the biotinylated protein can be detected by probing with labeled streptavidin. This technique has been used to investigate recombinant human **insulin** receptors expressed on the surface of murine NIH-3T3 cells. Biotinylation of the extracellular domain with an impermeant reagent did not impair the ability of an **antibody** directed against an epitope in the intracellular domain to immunoprecipitate **insulin** receptors. In contrast, biotinylation reduced the avidity of a polyclonal **antibody** directed against the extracellular domain of the receptor. Nevertheless, by increasing the concentration of the antireceptor **antibody**, it was possible to successfully immunoprecipitate the biotinylated receptor. Furthermore, biotinylated receptors retained the ability to bind **insulin** and undergo **insulin**- stimulated autophosphorylation and internalization. The use of enzyme- labeled streptavidin enables the use of **chemiluminescence** techniques to detect the receptors, thus obviating the need to employ radioactivity. Just as the technique is useful to study cell surface **insulin** receptors, it can be adapted to investigate other cell surface receptors and proteins.

L10 ANSWER 16 OF 16 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN  
ACCESSION NUMBER: 1991:21297268 BIOTECHNO  
TITLE: Chemiluminescent immunoassay for **insulin**  
AUTHOR: Yang X.; Guo A.; Wu L.; Deng A.; Yang H.  
CORPORATE SOURCE: China.  
SOURCE: Journal of West China University of Medical Sciences, (1991), 22/3 (259-261)

CODEN: HYDXET ISSN: 0257-7712  
DOCUMENT TYPE: Journal; Article  
COUNTRY: China  
LANGUAGE: Chinese  
SUMMARY LANGUAGE: English  
AN 1991:21297268 BIOTECHNO

L Number	Hits	Search Text	DB	Time stamp
1	5046	insulin.ti.	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:43
2	35	insulin.ti. and (c-peptide) and fluoresce\$4	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:36
3	4	(insulin.ti. and (c-peptide) and fluoresce\$4) and ((c-peptide) same fluoresce\$4)	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:36
4	32	insulin.ti. and (fluorescen\$4 same peptide)	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:43
5	13	insulin.ti. and (fluorescen\$4 same peptide same antibody)	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:48
6	53	insulin same (fluorescen\$4 same peptide same antibody)	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:56
7	12	RIA same fluorescen\$4 same insulin	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 16:20
8	59	insulin same chemiluminescen\$3 same antibody	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 16:21
9	29	(insulin same chemiluminescen\$3 same antibody) and @py<2002	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 16:21
10	15	(insulin same chemiluminescen\$3 same antibody) and insulin.ti.	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 16:21

L Number	Hits	Search Text	DB	Time stamp
1	5046	insulin.ti.	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:43
2	35	insulin.ti. and (c-peptide) and fluoresce\$4	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:36
3	4	(insulin.ti. and (c-peptide) and fluoresce\$4) and ((c-peptide) same fluoresce\$4)	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:36
4	32	insulin.ti. and (fluorescen\$4 same peptide)	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:43
5	13	insulin.ti. and (fluorescen\$4 same peptide same antibody)	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:48
6	53	insulin same (fluorescen\$4 same peptide same antibody)	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 15:56
7	12	RIA same fluorescen\$4 same insulin	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 16:20
8	59	insulin same chemiluminescen\$3 same antibody	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 16:21
9	29	(insulin same chemiluminescen\$3 same antibody) and @py<2002	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 16:21
10	15	(insulin same chemiluminescen\$3 same antibody) and insulin.ti.	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 16:21

L Number	Hits	Search Text	DB	Time stamp
1	0	("(c)near2peptide) sameinsulin").PN.	USPAT; US-PPGPUB; EPO; DERWENT	2004/05/21 10:00
2	0	("(c)near2peptide").PN.	USPAT; US-PPGPUB; EPO; DERWENT	2004/05/21 10:00
3	0	("(C-peptide) sameinsulin").PN.	USPAT; US-PPGPUB; EPO; DERWENT	2004/05/21 10:01
4	0	("insulinsameimpurity").PN.	USPAT; US-PPGPUB; EPO; DERWENT	2004/05/21 10:01
5	429	(c near2 peptide) same insulin	USPAT; EPO	2004/05/21 10:07
6	0	((c near2 peptide) same insulin) and H1A1	USPAT; EPO	2004/05/21 10:04
7	0	((c near2 peptide) same insulin) and (gly-arg-arg)	USPAT; EPO	2004/05/21 10:04
8	333	((c near2 peptide) same insulin) and (ph)	USPAT; EPO	2004/05/21 10:08
9	8	((c near2 peptide) same insulin) same soluble	USPAT; EPO	2004/05/21 10:06
10	71	((c near2 peptide) same insulin) and ((ph) same soluble)	USPAT; EPO	2004/05/21 10:08
11	14	((c near2 peptide) same insulin) and ((ph) near7 soluble)	USPAT; EPO	2004/05/21 10:08

L Number	Hits	Search Text	DB	Time stamp
14	5046	insulin.ti.	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 10:50
15	16	insulin.ti. and ((ph) near5 insoluble)	USPAT; US-PGPUB; EPO; DERWENT	2004/05/21 10:50